TRANSCELL BIOLOGICS

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KEYWORDS

Mesenchymal stem cells

Neuroregeneration and neurorestoration

Patient-derived stem cells

Drug-testing platforms

Induced pluripotent stem cells

Alzheimer's disease

Parkinson's disease

Amyotrophic Lateral Sclerosis

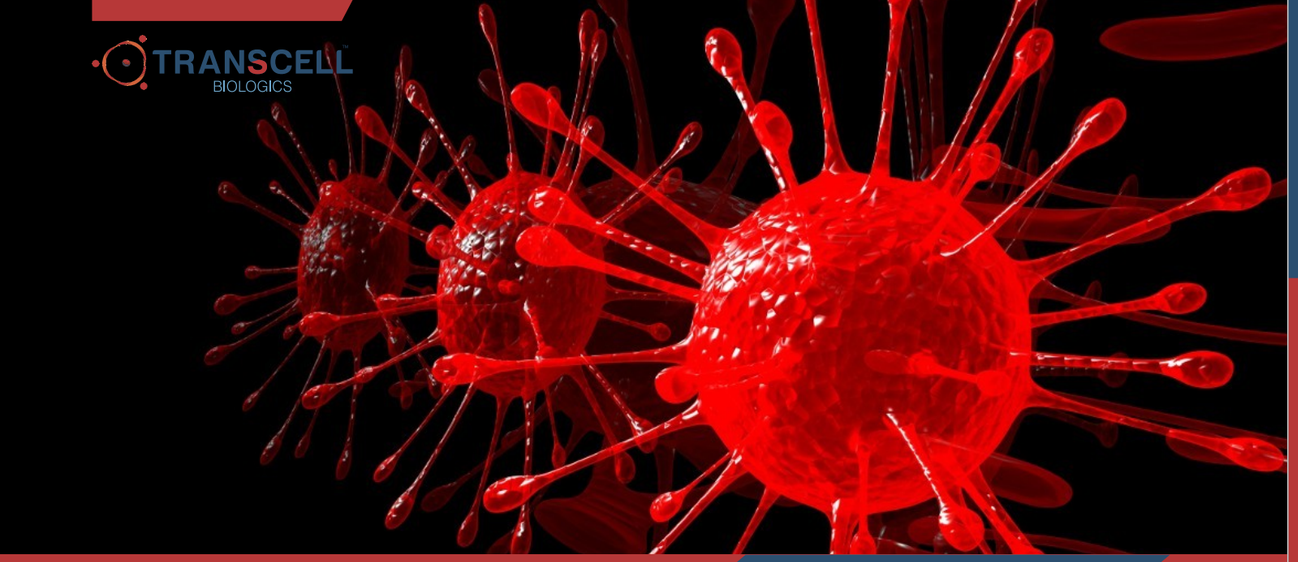
Stem Cell Biology As Century Of Biology For Drug Discovery In Neurological Disorders

Subadra Dravida C.E.O

New revelations into the biology of stem cells have raised expectations for their use in the treatment of neurologic diseases. Formerly, stem cell transplantation was promulgated as tools of replacing cells in central nervous system indicating that transplanted stem cells may decrease deleterious inflammation as well and improve endogenous recovery processes. Generally, neurodegenerative disorders are investigated using animal models, primary cultures and post mortem human brain tissues. The trans-differentiating properties of stem cells into different lineages including of ectodermal neurogenesis make them very fascinating advanced platforms for screening drug molecules property advantageous for neuroregeneration. This is to the extent of considering stem cell platforms for predicting drug molecules role towards specific target receptors of the brain cells. In December 2016 Transcomm, we critically appraise the different types of stem cells, their established therapeutic role, and the applications to which they have been attributed to, with the hope that the evidence shown on the stem cells be translated into clinical reality.

I want to highlight 2016 news on the 13-year study published in The Lancet showing stem cells' life-altering benefits for multiple sclerosis patients while wishing you all a happy reading and New year 2017.

Subadra



Patient-derived somatic cells (for example, fibroblasts) can be reprogrammed to generate iPSCs carrying a disease-specific genetic aberration. These cells can then be differentiated into the disease-affected cell type (for example, neurons in neurodegenerative diseases). After the establishment of a cellular disorder model with disease-specific phenotypes, three main strategies are commonly used: high-throughput screening (HTS) of drugs, the candidate drug approach or patient-specific therapy. In HTS, a very large number of compounds are tested on the differentiated cells, followed by phenotype re-evaluation. This method is extremely valuable for identifying novel therapies in vitro, by using large libraries of compounds. By contrast, both the candidate drug approach and the patient-specific therapy use a small number of potential drugs to attenuate the disease. These approaches are useful when the disease mechanism is known and potential therapies are available. Drugs found by both the HTS and candidate drug approaches usually require substantial safety assays before being prescribed to patients, whereas drugs already approved by regulatory agencies can be immediately prescribed for treatment.

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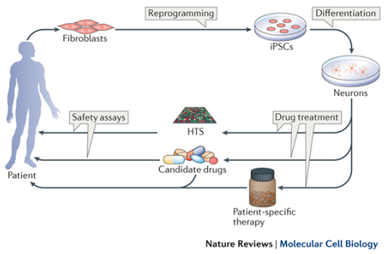

Nature Reviews | Molecular Cell Biology

Gene therapy using mesenchymal stem cells for Huntington's disease is showing promise in mouse studies, and preparations are underway to possibly move it into clinical testing. Before the technique might be ready for human trials, however, scientists need to master a few more steps, using larger animal models to investigate the therapy's safety and likely long-term effects. In the report, "Clinical trial perspective for adult and juvenile Huntington's disease using genetically-engineered mesenchymal stem cells, "published in the journal Neural Regeneration Research scientists at University of California Davis Health System summarize the advances so far, discuss the shortcomings of mouse models of Huntington's disease, and describe preparations for a future clinical trial. Because of their unique biological properties, mesenchymal stem cells have shown tremendous promise in stem cell-based gene therapy approaches in recent years, and applications targeting other neurological diseases, such as ALS and stroke, are now in clinical trials.
These stem cells can be isolated from several easily accessible tissues, and can migrate to brain areas of tissue damage, where they release beneficial factors of their own. They can also be easily manipulated to express other factors.

One of the most important features of these cells, making them such a valuable option for clinical practice, is that they do not elicit an immune response when transplanted from one person to another.

Stem cell-based gene therapy for Huntington's being readied for possible Human Trials

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Growing Popularity of the Global Stem Cell market

Unmet Medical Needs and Increasing Government Support Boost Global Stem Cells Market
With an ever increasing demand for medical intervention for growing chronic illnesses, the number of R & D activities in the field of mesenchymal stem cells has been rapidly growing. In developed countries like the US, improved government support and access to funding has been fostering stem cell based clinical research. The increasing awareness among the general public has also been adding to this surge in the market for stem cells.

Rapid proliferation of medical tourism facilities across countries such as India, Brazil, China, Malaysia, and Mexico also aids the development of the stem cells market in Latin America and Asia Pacific. Apart from the aforementioned market drivers, a multitude of factors present substantial growth opportunities before the market, such as rising disposable incomes in developing economies, development of the contract research industry, increasing prevalence of neurodegenerative diseases, and the need to replace animal tissue in drug discovery.
North America has been leading the global stem cells market in 2011, followed closely by Europe. High prevalence of neurological and cardiac diseases in the U.S, which, according to the Centers for Disease Control and Prevention, causes more than 50% of the total deaths in the country every year, is a significant factor contributing to the growth of the stem cells market in North America.

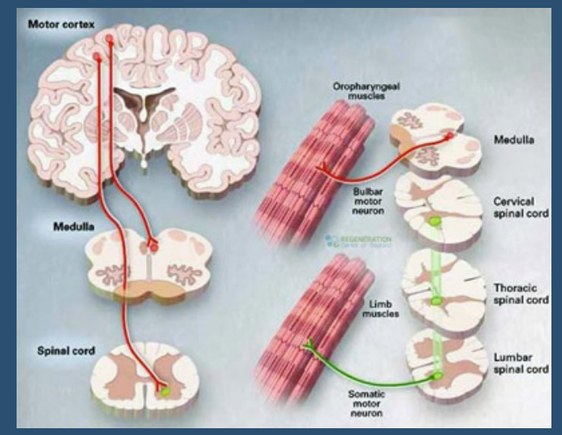
The literature analyzed:
It is observed that the neuro-restoration is evolving at an accelerated pace over the past decade. This report has briefly compiled the widespread applicability of stem cells and induced pluripotent stem cells to achieve neurorestoration. Overall, it is noticed that human stem cells and patient derived iPSCs have been instrumental in overcoming the major limitations of animal based research, providing a more profound understanding of the neurodegenerative disorders. Patient derived iPSCs are even better models for understanding the disease pathophysiology and mechanisms because they carry the patient's genotype, bear the disease mutations and also account for the environmental influences, thereby reducing variables to a large extent. Although it is agreed that stem cell therapy has set off both interests and alarms in the scientific community, its arrival has paved the way for a possible cure with minimized side effects. Personalized medical treatment using iPSCs is the current face of modern medicine and in the present context, less invasive methods of stem cell implantation across the blood brain barrier are being explored. Additionally, constant efforts are being made to scale down the cost and increase the efficacy of the approach.

Neurodegenerative diseases have a series of devastating consequences and the lack or curative therapies often have a high economic impact, thereby placing a huge burden on the society. This is becoming a global health concern. However, recent advances in stem cell biology are serving as a ray of hope, as they are changing the current face of neurodegenerative disease modelling, diagnosis and transplantation therapeutics.
(Marchetto et al., 2011). However, these techniques have their own limitations, although they are informative. By definition, Stem cells are the naive cells of the body with a commendable ability to self-renew, proliferate, differentiate into cells for multi-lineage commitment. Interestingly, their origin can either be fetal, embryonic or adult tissues of the body (iPSCs). Stem cells and iPSCs have been recently finding widespread applications, serving as disease models as well as transplantation and regenerative therapeutics. Every disease has its own characteristic parameter to evaluate- cellular, molecular, anatomical, genotypic and phenotypic attributes. To understand these aspects in vitro, very specific cell types expressing the disease phenotypes are a necessity. Fortunately, most of these requirements have been positively met by the use of stem cell technology.

ALZHEIMER'S DISEASE (AD)
Alzheimer's disease (AD) is one of the most prevalent neurodegenerative disorders of the world, lately reported as the 6th major reason for death. It is the leading cause of dementia in the aging population, as the hippocampus, amygdale, neocortex and basal forebrain regions of the patients' brains are adversely affected, leading to a severe impairment of cognition and memory. The tau hypothesis says that tau protein abnormalities initiate the very disease cascade. In this model, hyperphosphorylated tau begins to pair with other threads of tau forming neurofibrillary tangles inside nerve cell bodies. This leads to microtubules disintegration, destroying the structure of the cell's cytoskeleton collapsing the neuron's transport system. Using the mouse models of AD, Blurton-Jones et al in 2009 reported that neural stem cells transplanted in the hippocampus improved memory deficits significantly. Furthermore, observations from animal studies have pointed out that transplanted stem cells migrated and differentiated into cholinergic neurons, astrocytes, and oligodendrocytes. Apart from replacement of the lost neurons, stem cells stimulated endogenous neural precursors, promoted structural neuroplasticity, inhibited proinflammatory cytokines, suppressed neuronal apoptosis and expressed growth factors [Abdel-Salam, 2011]. Yagi et al(2011) is credited to have first derived neurons from patient iPSCs. Since then, a number of studies have been directed towards the approach of patient-specific iPSC derived AD modelling which have resulted in positive outcomes.

PARKINSON'S DISEASE (PD)
Parkinson's disease ranks second after AD in being the most common and widely prevalent neurodegenerative disorder inflicting almost 1% of the aging population globally. It is typically a disease of the basal ganglia characterized by a progressive degeneration of the dopaminergic neurons in the substantia nigra. This leads to motor dysfunction. The presence of lewy bodies (a-synuclein aggregates) which further promotes neural death is another major hallmark of this disease. The currently available therapies for PD only address the symptoms but do not cure the illness.
Over the last two decades, preclinical and clinical trials in PD patients have demonstrated that stem cell therapy of human embryonic mesencephalic tissue has the capacity to reinnervate the striatum. In fact, PD has emerged as the best-suited neurodegenerative diseases for stem cell therapy (Rosser et al., 2007 and Kim et al., 2009). The basic essence of stem cell therapy in PD is their ability to differentiate into dopaminergic neurons. Very encouragingly, Soldner and colleagues' finding in 2009 that fibroblasts from PD patients can be reprogrammed to differentiate into dopaminergic neurons was a turning point in the clinical area of PD. However, despite the impressive potential of stem cell therapy in PD, there is always a risk of the serious graft-induced dyskinesis involved, which are being carefully evaluated.

AMYOTROPHIC LATERAL SCLEROSIS(ALS)
ALS is a fatal neurodegenerative disease characterised by the death of the upper and lower motor neurons with subsequent muscular paralysis and atrophy. Compared to other neurodegenerative diseases, certain features of ALS make it more challenging to experiment stem cell therapy. The most important aspect is the unknown pathogenesis, followed by the lack of knowledge on how the disease spreads in the human body. Choosing the ideal site to implant stem cell is difficult without answers to the above questions. Theoretically, the objective of stem cell therapy in ALS would be to substitute the motor neurons. Further, the fundamental strategies of stem cell therapy in ALS consist of the regulation of inflammation and the expression of neurotrophic factors.
Transplantation therapy employing stem cells can be effectively used as a therapeutic measure to deal with the devastating disease. Mesenchymal stem cells and hematopoietic stem cells have been efficiently employed as transplants in the affected spinal cord and have favourably supported ALS management (Mazzini et al., 2012). However, studies were conducted on a small group of patients and thus thorough research continues so as to apply the same for a larger pool of patients. Neural stem cells (NSCs) Embryonic stem cells (ESCs), glial- restricted progenitor cells (GRPs), and induced pluripotent stem cells (iPSCs) also offer a potential alternative for transplantation approaches and can be used (Traub et al., 2011). Stem cell therapy has been an area of debate for a long time. The beneficial aspects cannot be overlooked, but extensive clinical trials are in progress so as to generate an effective treatment and possible cure for ALS in the near future.



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